

**REMARKS**

A Petition for Extension of Time is being concurrently filed with this Amendment. Thus, this Amendment is timely filed.

Applicant respectfully requests the Examiner to reconsider the present application in view of the foregoing amendments to the claims and the following remarks.

**Status of the Claims**

Claims 1 and 3-8 are currently pending in the present application. The Office Action is non-final. Claims 1, 3 and 4 have been amended without prejudice or disclaimer. No new matter has been added by way of the amendment, because the amendment is supported by the present specification. Claim 2 has been cancelled without prejudice or disclaimer. The amendment to the claims further defines and clarifies the structure of the present invention. Support for claim 1 can be found on page 5, lines 23, to page 6, line 9 of the present specification. Additionally, claim 3 support for "standard concentration" is based on the disclosure at page 13, lines 9 to 14 of the present specification. Also, the language of claims 3 and 4 were simplified as requested by the Examiner. Claim 6-8 are new. Support for claim 6 can be found on page 5, lines 23, to page 6, line 9 of the present specification. Support for claims 7 and 8 can be found on page 5, line 20 of the present specification. Thus no new matter has been added.

Based upon the above considerations, entry of the present Amendment is respectfully requested.

### ***Objection to the Specification***

The Examiner indicates that the specification was objected to due to informalities. Applicants have amended the specification, as requested by the Examiner, to correct the informalities of the use of trademarks, as well as correcting the last sentence in the last paragraph on page 5.

Applicants respectfully request reconsideration and withdrawal of the present objection.

### ***Claim Objections***

The Examiner states that claims 1-5 are objected to due to informalities. Applicants have amended claim 1, without prejudice or disclaimer, to include "...preparing a sample consisting essentially of a protein to be tested dissolved in water..." This amendment should obviate the objection to claim 1 and the claims that depend from claim 1.

Applicants have also cancelled claim 2, without prejudice or disclaimer, thus obviating this objection as well as other objections to claim 2 cited by the Examiner.

Lastly, the Examiner states that Claims 2-4 are objected to because they recite "a protein" which is ambiguous as to which protein Applicants are referring to. Also, the Examiner suggests that the antecedent basis for protein has been established in claim 1, and dependent claims should recite "the protein" or "said protein."

Applicants have amended claims 3 and 4, without prejudice or disclaimer, as requested by the Examiner. Within claim 3 and 4, "a protein" was amended to "the protein."

Applicants respectfully request reconsideration and withdrawal of the present objections.

***Rejection Under 35 U.S.C § 112, Second Paragraph, Indefiniteness***

Claim 4 stands rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicant regards as the invention.

The Examiner asserts that claim 4 is rejected as indefinite for omitting essential steps such as omission amounting to a gap between the steps, in which the omitted steps include a definition of a standard concentration to which the recited markers is to be adjusted to a concentration lower when compared. Applicants respectfully traverse.

As is indicated in the above Listing of Claims, claim 4 does not recite that which the Examiner asserts. Applicants believe that the Examiner may be referring to claim 3. Applicants have therefore amended claim 3, without prejudice or disclaimer, to add a definition for “standard concentration.” A skilled artisan (*e.g.*, a biochemist) would utilize the manufacturer’s stated concentration of a molecular marker and would know that based on the stated concentration that the skilled artisan would be able to dilute the molecular marker to a low concentration. Also a skilled artisan would also be able to employ a general protocol based on the concentration of the molecular weight marker with the kind of electrophoretic apparatus, the detection limit, the detection sensitivity and determination accuracy of the electrophoretic apparatus to be able to dilute the molecular weight marker to a low concentration. Therefore the rejection is overcome.

Applicants respectfully request reconsideration and withdrawal of the present rejection.

***Rejection Under 35 U.S.C. § 102(b), Anticipation***

Claims 1, 2, and 5 stand rejected under 35 U.S.C. § 102(b) as anticipated by Gordon *et*

*al.*, "Protocol for Resolving Protein Mixtures in Capillary Zone Electrophoresis," Analytical Chemistry, vol.63, no. 1, pp. 69-72,. ( 1991)(hereinafter "Gordon").

The Examiner asserts that Gordon discloses a protocol for resolving protein mixtures using capillary zone electrophoresis and teaches preparation of a sample comprising proteins of interest in water for electrophoretic protein separations. The Examiner also asserts that the proteins separated from the mixture in Gordon were not heat denatured in the stated protocol and that Gordon teaches the use of capillary zone electrophoresis as the method of electrophoresis. Applicants respectfully traverse.

The Examiner notes that Gordon teaches the preparation of a sample comprising proteins of interest in water. However, more exactly, it is described within Gordon that the separation of protein mixtures by capillary zone electrophoresis can be plagued by wall adsorption of the protein components, causing peak broadening and distortion, and that Gordon resolves this problem by presenting a method for overcoming this problem by adding ethylene glycol to the protein sample (see Gordon, page 69, abstract). More specifically, Gordon describes that the "the sample was prepared by mixing together the following three components in the ratio 1:3:1, namely, proteins of interest in water, 20mM boric acid (pH 4.0), and ethylene glycol" (see Gordon, page 70-CZE Run Conditions). That is, in addition to water, boric acid and ethylene glycol are contained in a sample of Gordon.

In contrast, in the present invention as defined by the amended claims, a protein of interest is dissolved in a solution that does not contain ethylene glycol and/or boric acid so that the present invention is different from Gordon. In addition, the claims further require that the pH of the sample is 2.0 to 9.0. In contrast, Gordon indicates that:

*"In order to understand better the contributions of ethylene glycol and alkaline pH (pH 10.0), a serum sample was run five times with the ethylene glycol. The resulting electropherograms show excellent reproducibility for retention time and peak area. The same sample was run five times under the same conditions but without the ethylene glycol. The first run has most of the peaks separated. The second through fifth runs show the retention times increasing with run number and the peak areas changing from run to run. In other words, without ethylene glycol in the protein sample the electropherograms are not reproducible. When a serum sample with ethylene glycol is run in a barbitol buffer, pH 8.6, the separation of peaks, as detected by UV absorption at 280 nm, is unsatisfactory, but that pattern is very reproducible in subsequent runs. However, if the sample without ethylene glycol is run in the same buffer, the electropherogram is similar to the runs with ethylene glycol, but the second run shows marked distortion of the pattern, which worsens with subsequent runs."* (see Gordon at page 72, first column, first paragraph).

One control experiment (without ethylene glycol) was run at pH 10 as indicated above in borate buffer and therefore the claims are distinguishable from this control experiment based on the pH limitation.

Because "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference," the cited Grigoriev '965 reference cannot be a basis for a rejection under § 102(b). See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus,

because of the lack of disclosure of all features as instantly claimed, the rejection in view of Gordon is overcome. Since the independent claim 1 is not anticipated by Gordon, the dependent claims are also not anticipated. Applicants respectfully request reconsideration and withdrawal of the present rejection.

***Rejection Under 35 U.S.C. § 103(a), Obviousness***

Claims 3 and 4 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gordon in view of Tadayoni-Rebek *et al.*, U.S. Patent Application Publication No. 2002/0155455 (hereinafter “Application ‘455”).

The Examiner asserts that Gordon discloses the limitations recited in claim 1 as outlined in the previously discussed 35 U.S.C. § 102(b) rejection. The Examiner admits that Gordon does not disclose molecular weight markers subject to electrophoresis together with a protein, as recited in claims 3 and 4.

Further the Examiner asserts that Application ‘455 discloses high homogeneous molecular markers for electrophoresis, teaches marker molecules comprising a collection of two or more marker molecules, and teaches the addition of the marker molecule composition to a sample containing protein.

Additionally the Examiner asserts that at the time of the present invention, it would have been obvious to one of ordinary skill in the art to modify the Gordon protocol with the utilization of molecular weight markers taught by Application ‘455 because doing so allows one to obtain highly homogeneous visible molecular markers that are compatible with commercially available separation techniques. Applicants respectfully traverse.

Reconsideration and withdrawal of this rejection is respectfully requested based on the following considerations.

*Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), has provided the controlling framework for an obviousness analysis. A proper analysis under § 103(a) requires consideration of the four *Graham* factors of: determining the scope and content of the prior art; ascertaining the differences between the prior art and the claims that are at issue; resolving the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467.

The U.S.P.T.O. published a set of Obviousness Guidelines titled: “Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*” (See, Fed. Reg. 72(195):57526-57535, October 10, 2007). This publication provides a review of the factors to be considered under the test announced in the *Graham v. John Deere* holding. These Obviousness Guidelines re-affirm the validity of the TSM test in determining obviousness, as well as the factor test of *Graham v. John Deere*.

Applicants incorporate by reference the above remarks for the 35 U.S.C. § 102(b) rejection and apply them to the present rejection. As to the present rejection, Gordon as a primary cited reference does not teach the feature of the present invention as noted above so that the present invention is not obvious even in consideration of Application ‘455, because Application ‘455 also fails to teach the feature. The effects of the present invention are described in the specification, for example, at Example 1, and especially at page 19, lines 11-13 and Figure 1.

In contrast, Gordon indicates:

*...The recent technology of capillary zone electrophoresis (CZE) has been shown to separate many types of molecules quickly and efficiently....Jorgenson and Lukacs...noted in the early stages of (CZE) development that proteins posed a particular problem; i.e., many proteins had a tendency to stick to the walls of the capillary. The resulting slow adsorption and desorption kinetics caused extensive tailing in the protein peaks. (See Gordon, Introduction).*

Gordon shows that in capillary electrophoresis, that at the time, the use of a protein without ethylene glycol posed problems with proteins adhering to the capillary wall and causing detrimental effects to electrophoretic performance.

In fact Gordon, as discussed above, teaches away from the present invention since Gordon indicates that “*...without ethylene glycol in the protein sample the electropherograms are not reproducible.*” (see Gordon at page 72, first column, first paragraph).

Any cited reference used for a rejection under 35 U.S.C. § 103(a) must be considered in its entirety, i.e., as a whole, including those portions that would lead away from a claimed invention. See *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). In other words, the Gordon reference must be read in its entirety, including the teaching away that not using ethylene glycol and borate buffer would have negative effects on reproducibility and electrophoretic performance.

Based upon the above, and applying the *Graham factors* analysis test or a test described within the Guidelines, it is submitted that a *prima facie* case of obviousness has not been established as to the pending claims. “[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR*, quoting *In re Kahn*,



441 F.3d 977, 988 (CAFC 2006). Therefore, in light of the above, it is submitted that the Examiner did not meet the standard for a *prima facie* case of obviousness.

Applicants respectfully request reconsideration and withdrawal of the present rejection.

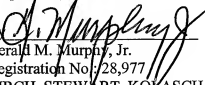
In view of the above, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Paul D. Pyla, Reg. No. 59,228, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.147; particularly, extension of time fees.

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Respectfully submitted,

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